Medical Journal of the
Islamic Republic of Iran

Volume 11
Number 4
Winter 1376
February 1998

THE OCCURRENCE OF ENDOMETRIOSIS AMONG INFERTILE PATIENTS WITH UTERINE MYOMA AND THOSE WITH POLYCYSTIC OVARIAN DISEASE: COMPARISON WITH INFERTILE CONTROL CASES

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ABSTRACT

In order to determine the occurrence of endometriosis in patients with uterine myoma and in those with polycystic ovarian disease (PCOD) compared to controls, 540 infertile patients were first divided into two age groups of 20-29 and 30-39. Then each group was subdivided to patients with 1) uterine myoma, 2) PCOD, and 3) no uterine myoma or PCOD (control subgroup). The occurrence of endometriosis was ascertained in each subgroup. This occurrence was compared between subgroups 1 and 3, and subgroups 2 and 3. For statistical analysis the Mantel and Haenszel test was used.

The occurrence of endometriosis in general was higher in subgroup 1 than in 3 (45.9% versus 19.9%), and the Mantel and Haenszel test gave a $p<0.002$. The occurrence of endometriosis was lower in subgroup 2 than in 3 (7.3% versus 19.9%), and the Mantel and Haenszel test gave a $p<0.005$.

As it is classically stated that myoma is an estrogen dependent tumor and PCOD patients have an androgenic milieu, it could be suggested that the different effects of hormones may be the reason for the varied occurrence of endometriosis found in this study.

MJIRI, Vol. 11, No. 4, 315-317, 1998.

INTRODUCTION

The occurrence of uterine myomata in patients with pelvic endometriosis is reported to be nearly 15%.[1] The occurrence of adenomyosis in patients with uterine myoma has been mentioned previously,[2] and there is at least one report on the occurrence of endometriosis in patients with uterine myomas.[3]

Polycystic ovarian disease (PCOD) and pelvic endometriosis are both important causes of infertility. Babakniaetal.[4] found the occurrence of pelvic endometriosis in patients with PCOD to be 2.8%.

In the present study the occurrence of endometriosis was determined in patients with uterine myoma and in cases with PCOD and the results were compared with a control group.

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PATIENTS AND METHODS

This retrospective study was performed between May 1988 and August 1995 in Mirza Kouchek Khan Hospital, affiliated to Tehran University of Medical Sciences. Infertile patients who were examined via laparoscopy were initially included in this study (n= 651). The same physician performed all laparoscopies and the hysteroscopies that routinely preceded them.

Among the patients under study, there were no cases with PCOD older than 39 years of age and there was only one case with uterine myoma younger than 20, so only patients between 20-39 years were chosen for further study (n= 540). In addition, as patients with PCOD are usually younger than patients with uterine myoma, in order to decrease the possibility of age being a confounding variable, the patients were divided into two groups, those aged from 20-29 years and those between 30-39 years of age. In each group patients were divided into subgroup 1, uterine myoma; subgroup 2, PCOD; and subgroup 3, no uterine myoma or PCOD (control cases). The occurrence of endometriosis was ascertained in patients with uterine myoma and control cases and afterwards in patients with PCOD and control cases. Patients with co-existing uterine myoma and PCOD were omitted from the study as there were only 5 cases and analysis could not be subject to statistical analysis. Also, cases with symmetrical enlargement of the uterus were not included in the uterine myoma subgroup if they did not have a pathological report (5 cases). In the latter patients the differential diagnosis with adenomyosis was difficult. The subdivision of myomas according to the location was as follows: 39 subserosal, 8 submucosal, 2 intramural, 6 (subserosal + intramural), 2 (subserosal + submucosal), 2 (subserosal + intraligamental) and 2 intraligamental.

PCOD was established when, besides infertility, three of the four signs and symptoms below were present: 1) hirsutism, 2) menstrual abnormality (oligomenorrhea or amenorrhea), 3) body mass index>25, and 4) presence of a typical polycystic ovary on sonography. Laboratory findings of LH/FSH>2 (both measured in the early follicular phase) and/or total testosterone levels above normal were also essential.

During the operation the pelvis was carefully examined by a laparoscopist who was familiar with patterns of endometriosis (such as bluish-gray nodules and/or the presence of pigmented "powder burn" lesions...). The revised American Fertility Society classification for endometriosis staging had been in the patients' medical files.[5]

For statistical analysis the Mantel-Haenszel test (for combining data over two age groups) was used.

RESULTS

Stages of endometriosis in patients with uterine myoma were as follows: stage I (n=14), stage II(n=8), stage III(n=4), and stage IV(n=2). Among PCOD patients, there were four cases with endometriosis in stage I and one in stage II.

Table I. Occurrence of endometriosis by age and diagnosis.

Age	Myoma	PCOD	Control
20-29	6/17 (35.3%)	4/50 (8%)	44/261 (17.6%)
30-39	22/44 (50%)	1/18 (5.5%)	38/150 (25.3%)
Total	28/61 (45.9%)	5/68 (7.3%)	82/411 (19.9%)

- Myoma versus control, $p<0.002$.
- PCOD versus control, $p<0.005$

Table I shows that in both age groups, the highest occurrence of endometriosis was found in patients with uterine myoma and the lowest occurrence in PCOD patients.

In statistical tests which were used for comparing the occurrence of endometriosis in subgroups 1 and 3 and subgroups 2 and 3, the occurrence in subgroup 1 was higher than in 3 ($p<0.002$) and in subgroup 2 was lower than in 3 ($p<0.005$).

DISCUSSION

The occurrence of endometriosis in control cases of the present study was 19.9%. This figure was close to the lower limit of occurrence of endometriosis in infertile patients which has been previously reported (21-46%).[6-7]

The present literature is not rich in information concerning the occurrence of endometriosis in patients with uterine myoma. In this study it was found that the prevalence of endometriosis was higher in patients with uterine myoma than in the control cases (Table I).

The overall occurrence of endometriosis in infertile patients with PCOD in our study was 7.3%. The occurrence of endometriosis in PCOD patients in other articles was reported to be 16.5%[8], 6%[9], and 2.8%[4]. In the first two reports, similar to our study, the diagnosis of endometriosis was made by laparoscopy. The incorporation of control cases gave significance to our findings.

Clinical observations and animal data suggest that an estrogenic milieu may be necessary for the initial neoplastic transformation of myometrial cells into a myoma.[10] Investigators have demonstrated a higher intra-myoma estrogen environment when compared to the myometrium of the same uterus.[11-12] It was also stated that androgens can cause atrophy of endometrial implants,[13] and PCOD patients usually have an androgenic milieu.[14] Therefore, it could be suggested that the different effects of hormones may be the reason for the varied occurrence of endometriosis found.

Barbieri[15] mentioned an estrogen threshold hypothesis

in which the blood estrogen levels should increase to a special point before affecting the endometrial implant. With this view, patients with endometriosis, when under treatment with GnRH-agonists, can be given a low dose of estrogen for prevention of osteoporosis without any effect on the endometrial implant.[15] However, the findings in this study suggest an "interactional hormonal threshold hypothesis". This means that in natural conditions the threshold of hormonal effects on endometrial tissue may be dependent upon the opposing hormonal effects and not the estrogen effect alone. According to this new hypothesis, if a patient has a higher level of androgens, a higher amount of estrogen can be given before reaching that threshold.

The control group might be criticized as harboring patients with hypothalamic amenorrhea or premature ovarian failure (both with low estrogen milieu) and other PCOD patients not included in the PCOD definition used in this study (possibly with an androgenic milieu). Consequently, according to the proposed hypothesis, these subjects would falsely cause the occurrence of endometriosis to be low. But, after omitting the above groups (14 with hypothalamic amenorrhea and premature ovarian failure with no case of endometriosis, and 80 with polycystic ovaries upon laparoscopy with 10 cases of endometriosis), the statistical significance of the occurrence of endometriosis in the control group was unaffected (72/317= 22.7% versus 82/411=19.9%).

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